Regimen Monograph

A - Regimen Name

FLUD(PO) Regimen

Fludarabine (oral)

Disease Site	Hematologic - Lymphoma - Non-Hodgkin's Low Grade (including Waldenstrom's Macroglobulinemia)
Intent	Palliative
Regimen Category	**Evidence-Informed :** Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.
Rationale and Uses	Second-line therapy for previously treated patients with stage III-IV low-grade lymphoma (including Waldenstrom's Macroglobulinemia)

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B - Drug Regimen

fludarabine	40 mg /m²/day	PO	Days 1 to 5

(This drug is not currently publicly funded for this regimen and intent)
(Outpatient prescription available in 10mg tablets)

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C - Cycle Frequency

REPEAT EVERY 28 DAYS

For a total of 6 cycles, or 2 cycles beyond maximum response in the absence of disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal

Other Supportive Care:

- Allopurinol and hydration to reduce the risk of tumour lysis syndrome are recommended.
- Consider prophylaxis for PCP (cotrimoxazole) as per local guidelines.
- Use irradiated blood products to ↓ risk of GVHD.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations are in use at some centres.

Dosage with toxicity

Hematologic Toxicities: See Appendix 6 for general recommendations.

Toxicity / Grade	Action	Dose next cycle
Platelet < 100 x 10^9/L and/or ANC < 1.5 x 10^9/L	Hold until recovery	↓ 25%
Febrile neutropenia, thrombocytopenic bleeding	Hold until recovery	↓ 25%
Grade 3 non-hematologic toxicity	Hold until recovery	↓ 25%
Grade 4 non-hematologic toxicity OR Any grade neurotoxicity, hemolysis OR Suspected/proven pneumonitis/fibrosis	Discontinue	Discontinue

Hepatic Impairment

No data available; use with caution.

Renal Impairment

Creatinine Clearance	% usual dose
30 - 70 mL/min	REDUCE to 50%
< 30 mL/min	DISCONTINUE

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F - Adverse Effects

Refer to fludarabine drug monograph(s) for additional details of adverse effects

Most Common Side Effects	Less Common Side Effects, but may be Severe or Life Threatening
• Myelosuppression • Infection; including opportunistic • GI (nausea/vomiting, stomatitis, diarrhea) • Fever • Fatigue • Rash (may be severe) • Visual changes	• Autoimmune disorders (e.g.hemolytic anemia, TTP) • Tumour lysis syndrome • Encephalopathy, CNS toxicity (e.g. seizures, confusion, agitation) • Pulmonary fibrosis/pneumonitis • MDS (with alkylating agents) • Bleeding • Heart failure, angina

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G - Interactions

Refer to fludarabine drug monograph(s) for additional details

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H - Drug Administration and Special Precautions

Refer to fludarabine drug monograph(s) for additional details

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- Clinical toxicity assessment (including fever or infection, hemolysis, dehydration, pulmonary, GI, CNS).
- CBC before each cycle. Interim counts should be done in first cycle and repeated if dose modification necessary.
- Baseline and regular liver and renal function tests
- Creatinine clearance if > 70 yrs or renal dysfunction suspected

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration

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K - References

Boogaerts MA, Van Hoof A, Catovsky D, et al. Activity of Oral Fludarabine Phosphate in Previously Treated Chronic Lymphocytic Leukemia J Clin Oncol,2001; 19(22): 4252-4258

Fludarabine drug monograph, Cancer Care Ontario.

Klasa R, Meyer R, Shustik C, et al. Randomized phase III study of fludarabine phosphate versus cyclophosphamide, vincristine, and prednisone in patients with recurrent low-grade non-Hodgkin's lymphoma previously treated with an alkylating agent or alkylator-containing regimen. J Clin Oncol. 2002 Dec 15;20(24):4649-54.

Tobinai K, Watanabe T, Ogura M, et al. Phase II study of oral fludarabine phosphate in relapsed indolent b-cell non-hodgkin's lymphoma. JCO 2006; 24: 174-80.

June 2017 added not publicly funded to drug regimen

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M - Disclaimer

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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